RATIONALE FOR THE DEVELOPMENT OF ONTARIO AIR STANDARDS FOR CARBON TETRACHLORIDE

CONSULTATION DRAFT

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Executive Summary

The Ontario Ministry of the Environment has identified the need to develop and/or update air quality standards for priority contaminants. The Ministry's Standards Plan which was released in October 1996, identified candidate substances for the development of air standards for the next several years. Carbon tetrachloride was identified as a priority for review based on recent toxicological information published since the existing standard was developed in 1983.

Carbon tetrachloride is a colourless, clear, heavy liquid that readily vapourizes at room temperature. Its primary use is in the manufacture of fluorocarbon propellants. Because of its toxicity and potential to destroy the ozone layer, its use as a general industrial and commercial solvent has been severely restricted. The Federal Ozone Depleting Substances Regulations have targeted carbon tetrachloride for a complete phase-out by the year 2000. Exemptions to these regulations are for use as a feedstock in the manufacture of certain chemicals and as a laboratory standard.

Levels of carbon tetrachloride measured in Ontario are low with annual averages concentrations of about 1 $\mu g/m^3$ (microgram of carbon tetrachloride per cubic metre of air), a level comparable to that reported for rural areas worldwide, approximately 0.8 $\mu g/m^3$.

Based on human and animal studies, carbon tetrachloride is toxic via inhalation and ingestion causing damage to the central nervous system, kidneys and liver. Damage to the liver has been extensively studied in humans and numerous animal species and appears to be the most sensitive end-point. Evidence of human carcinogenicity, based on epidemiological studies, is not sufficient to arrive at any firm conclusions. In animal studies, carbon tetrachloride was shown to produce liver tumours at levels of exposure which produced significant liver damage. Carbon tetrachloride is classified as a probable human carcinogen (Group B2) by the United States Environmental Protection Agency and possible human carcinogen (Group 2B) by the International Agency for Research on Cancer (IARC) based on sufficient evidence in animals and inadequate evidence in humans.

The current Ontario air standards for carbon tetrachloride are as follows: the interim half-hour Point-of-Impingement standard is 1800 $\mu g/m^3$, while the 24-hour Average Ambient Air Quality Criterion is 600 $\mu g/m^3$. Based on recent toxicological information, the current Ontario standards, developed in 1983 are now considered to be in need of review.

In developing air quality standards for Ontario, the Ministry of the Environment is reviewing and considering air quality guidelines and standards used by environmental agencies world-wide. Of the criteria reviewed from other agencies, those of the California Department of Health Services were judged to have the most appropriate rationale. That agency has proposed a chronic Reference Exposure Level of 2.4 $\mu g/m^3$ (24-hour average) which is based on the Reference Dose established by the United States Environmental Protection Agency.

Based on an assessment of ambient air quality guidelines used in other jurisdiction; the levels of carbon tetrachloride measured in Ontario; modelled ground level concentrations from recent applications for Certificates of Approval; the Ministry is proposing to establish:

- a 24-hour Ambient Air Quality Criterion of 2.4 $\mu g/m^3$ to replace the current 24-hour AAQC of 600 $\mu g/m^3$;.

- a point of impingement guideline of 7.2 $\mu g/m^3$ to replace the existing interim point of impingement standard 1800 $\mu g/m^3$. The point of impingement guideline is based on the proposed 24-hour Ambient Air Quality Criterion and will be used to review and assess applications for Certificates of Approval involving emissions of carbon tetrachloride from new or modified sources.

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1.0 Introduction

Ontario's primary approach to regulating air emissions is based on achieving and maintaining air quality which is protective of human health and the environment. The *Environmental Protection Act* requires all stationary sources which emit or have the potential to emit a contaminant to obtain a Certificate of Approval which outlines the conditions under which the facility can operate.

Compliance with air quality standards and guidelines is one of the criteria used to issue Certificates of Approval. Sources or potential sources of a contaminant are required to control emissions to ensure that the concentration of a contaminant specified by the standard is not exceeded at any point off their property. Dispersion modelling which incorporates detailed engineering calculations is used to relate emission rates from a source to resulting ambient concentrations of a particular contaminant.

The Ministry of the Environment uses a combination of regulatory standards, ambient air quality criteria (AAQCs) and point of impingement (POI) guidelines in reviewing Certificates of Approval (MOEE, 1994a). Point of impingement standards are established under Regulation 346 and can be used directly as enforcement tools as the regulation specifies that a source cannot emit a contaminant at a level which would result in a standard being exceeded at its maximal point of impingement off its property (Section 5(3)). All sources are required to comply with Regulation 346 POI standards unless they are specifically exempted in regulation. As POI standards specified under Regulation 346 apply to all sources, socio-economic issues need to be taken into consideration in their development to ensure that the standards are technically feasible and there is a balance between the benefits and costs of improved ambient air quality.

In addition to POI standards established under Regulation 346, the Ministry also has a larger number of ambient air quality criteria and point of impingement guidelines which are derived from AAQCs. These are used by the Ministry to assess general air quality and the *potential* for causing an adverse effect (MOEE 1994). Like POI standards specified in Regulation 346, point of impingement guidelines are also used in Certificates of Approval to approve new and modified emission sources. Once incorporated into a legal instrument like a Certificate of Approval, point of impingement guidelines are legally binding, however unlike Regulation 346 POI standards, they do not automatically apply to existing sources at the time they are promulgated. AAQCs are normally set at a level not expected to cause adverse human health or environmental effects based on continuous exposure. As such, socio-economic factors such as technical feasibility and costs are not explicitly considered when establishing such limits.

Generally, point of impingement standards and guidelines which employ half-hour averaging times are set to ensure that if there is compliance with the standard or guideline, the Ambient Air Quality Criterion which is based on longer term averaging periods (e.g. 24-hours) will not be exceeded. In certain cases where the effect can occur over short-term exposures, like odours, the

24-hour Ambient Air Quality Criterion and the half-hour point of impingement standard may have the same value.

The Ontario Ministry of the Environment has identified the need to develop and/or update air guidelines/standards for priority toxic contaminants. The Ministry's Standards Plan which was released in October 1996, identified candidate substances for the development of air standards for the next several years. Carbon tetrachloride was identified as a priority for review based recent toxicological information published since the existing standards were developed in 1983. This document provides the rationale for recommending a revised AAQC and a point of impingement guideline for carbon tetrachloride.

2.0 Review and Evaluation

2.1 General Information

Carbon tetrachloride (CCl_4), also known as tetrachloromethane, is a colourless, clear, heavy liquid that readily vapourizes at ambient temperatures. Carbon tetrachloride which is the most toxic of the chloromethanes, is non-flammable, miscible with most organic liquids, and is a powerful solvent (UNEP, 1997). The Chemical Abstracts Service (CAS) identification number is 56-23-5, the Registry of Toxic Effects of Chemical Substances (RTECS) number is FG4900000 and the United Nations Hazardous Material number is UN1846. Its odour threshold is greater than 10 ppm (62 mg/m^3). Because of its toxicity and ability to deplete stratospheric ozone, its use has been severely restricted and it has been replaced in most of its traditional applications as a general industrial solvent and for dry-cleaning.

The most common effect of chronic exposure to carbon tetrachloride is liver damage. This damage has been extensively studied in humans, monkeys, rats, mice, rabbits, guinea pigs, hamsters, cats, dogs, sheep and cattle. These studies have shown that carbon tetrachloride induces centrilobular necrosis and fat accumulation in the liver. A progression of cellular damage, damage to sub-cellular structures and the accumulation of fatty material within the cells and tissue have been observed repeatedly. The extent of injury varies with species, age and sex. The exact mechanism of toxicity on the cellular level has not been identified, but the production of toxic metabolites seems to be the most commonly cited mechanism. Differences in metabolism may thus explain the variation in toxicity within and between species. A complicating factor is the potentiation of toxicity by alcohol consumption.

2.2 Sources and Levels

The 1995 National Pollutants Release Inventory lists 2 sources with atmospheric releases of carbon tetrachloride in Ontario. The largest of these, a chemical company located in Cornwall released a total of 5.61 tonnes. Subsequent to the 1995 reporting year, the production and use of carbon tetrachloride by this facility was discontinued.

An analysis of the applications from current Certificates of Approval in Ontario identified 16 sources with emissions of carbon tetrachloride covered by a Certificate. The majority of these approvals were for minor sources covering emissions from chemical fume hoods. The median Ground Level Concentration (GLC) predicted by Regulation 346 dispersion modelling for all 16 sources was approximately 6.35 $\mu g/m^3$ with the GLC from the individual sources ranging between 0.18 to 804.6 $\mu g/m^3$. The largest ground level concentrations were predicted for the installation of cryogenic heat extraction equipment at a facility which produces industrial gases.

Unless there is a nearby emission source, the levels of carbon tetrachloride measured in Ontario are low, usually below 2 $\mu g/m^3$ and annual averages are about 1 $\mu g/m^3$ or less (MOEE, 1994b). According to the Hazardous Substances Database (HSDB) (1996), carbon tetrachloride values in air samples from rural areas world-wide are reported to range from 0 to 0.13 ppb (approx. 0.8 $\mu g/m^3$). Air samples from urban areas are reported to range from 0 to 42.4 ppb (approx. 260 $\mu g/m^3$) while samples from industrialized areas have been measured at up to 70 ppb (approx. 400 $\mu g/m^3$).

2.3 The Control of Carbon Tetrachloride as an Ozone Depleting Substances

In accordance with the *Montreal Protocol on Substances that Deplete the Ozone Layer*, the federal government has introduced regulations which restricts use of carbon tetrachloride as an industrial solvent (SOR/93-214). Effective January 1, 2000 the only permitted uses of carbon tetrachloride which is not otherwise recovered or recycled are as a feedstock in certain chemical processes and as an analytical standard. The Montreal Protocol defines a feedstock as "...a substance that undergoes a transformation in a process in which it is converted from its original composition except for insignificant trace emissions as allowed." Feedstock uses include the use of carbon tetrachloride as a chloride donor in the production of certain products such as vinyl chloride monomer and chlorinated rubbers and plastics. Under the Montreal Protocol, the United Nations Environmental Program is assessing the range of industrial processes in which controlled substances are still in use in order to assess the feasibility of alternatives and substitutes.

2.4 Review of Existing Air Quality Regulations.

Agency-specific summaries of information concerning air quality guidelines for carbon tetrachloride are presented in the Appendix of this report. A brief summary is presented in Table 1.

Table 1. Summary of Existing Air Quality Guidelines[1] for Carbon Tetrachloride

Agency, Date[2]	**Guideline(s)**[3]		**Comments**
USEPA (IRIS) 1991	0.7 µg/m^3	(lifetime exposure)	1*10^{-5} additional cancer risk
	0.07 µg/m^3	(lifetime exposure)	1*10^{-6} additional cancer risk cancer risk based on unit risk of 0.000015 tumours/(µg/m^3)
California 1992	190 µg/m^3 2.4 µg/m^3	(1-hour average) (inhalation reference exposure level)	Acute reference level based on irritation and occupational exposure limits; inhalation reference exposure to be used for evaluation of non-cancer risk
	0.24 µg/m^3 0.024 µg/m^3	(lifetime exposure) (lifetime exposure)	1*10^{-5} additional cancer risk 1*10^{-6} additional cancer risk both are based on a unit risk of 0.000042 tumours/(µg/m^3)
WHO 1987	None		
Netherlands 1987	1 µg/m^3 60 µg/m^3	(target value) (maximum permissible concentration)	Based on risk assessment in Dutch; working multimedia harmonized guidelines.
Sweden	None		
New York 1990	1,300 µg/m^3	(1-hour average)	1-hour average based on occupational exposure limits;
	0.07 µg/m^3	(annual average)	1*10^{-6} additional cancer risk based on unit risk of 0.0000143 tumours/(µg/m^3)
Massachusetts 1990	85.52 µg/m^3	(24-hour ceiling limit)	24-hour average based on occupational exposure limits;
	0.07 µg/m^3	(allowable ambient limit)	1*10^{-6} additional cancer risk based on unit risk of 0.000015 tumours/(µg/m^3)
Ontario (current) 1983	1,800 µg/m^3 600 µg/m^3	(1/2-hour point of impingement limit) (24-h average AAQC)	Air quality standards based on human health considerations.

1. Guidelines in this table can refer to: guidelines, risk-specific concentrations based on cancer potencies, and non-cancer-based reference concentrations.
2. Date here refers to when the health-based guideline background report or original legislative initiative was issued. The sources were the respective agency documents.
3. 1 μg/m^3 ~ 0.151 ppb @ 1 atm. and 10 $^\circ$C

3.0 Development of an Ambient Air Quality Criterion for Ontario

3.1 Discussion of Regulatory Approaches for Carbon Tetrachloride

The regulation of long-term exposure to carbon tetrachloride in air can be based on two approaches, those based on the avoidance of injury to the liver and those based on the avoidance of cancer. The two approaches are examined separately.

3.1.1 Regulatory Approaches for Carbon Tetrachloride Based on Carcinogenicity

Carbon tetrachloride is classified by the United States Environmental Protection Agency as a probable human carcinogen (B2) and the International Agency for Research on Cancer as a possible human carcinogen (Group 2B) based on sufficient evidence in animals studies and inadequate evidence in humans (USEPA, 1991; IARC, 1987). There are several studies which demonstrate that carbon tetrachloride is carcinogenic to laboratory animals. All are based on oral exposure. According to the USEPA, the four studies that could be used to make quantitative risk estimates were all deficient in some respect, precluding the choice of any one study as most appropriate. In two studies, Della Porta *et al.* (1961) and Edwards *et al.* (1942), only one dose was tested. Della Porta *et al.* (1961) also did not report concurrent control incidence. In two National Cancer Institute studies, tumour incidence in the mice was virtually 100%, and goodness-of-fit criteria were not satisfied for the multistage model, the model typically used by the USEPA for extrapolation of unit risk to humans from animal models (NCI, 1976; 1976a). Tumour incidence in rats in these same studies was observed to be higher at low doses because of the mortality at the highest dose. The USEPA developed their unit risk estimate of $1.5*10^{-5}$ per $\mu g/m^3$ from the geometric mean of the four studies.

California (CARB, 1986) conclude that data from the Della Porta *et al.* (1961) study with hamsters and the NCI (1976; 1976a) study with rats were inadequate for use in calculating a unit risk. Rather than calculating a geometric mean, they instead reported separate unit risks of $4.2*10^{-5}$, using the Edwards *et al.* (1942) data on mice and $9.9*10^{-6}$ using the NCI (1976; 1976a; 1977) data on mice. California selected the unt risk value from the Edwards *et al.* study because of deficiencies in experimental design of the NCI study. They also used different values for converting oral doses to inhalation doses for the animals and a higher absorption factor for carbon tetrachloride in humans. Both CARB (1986) and the USEPA (1995), in reviewing data on mutagenicity, conclude that carbon tetrachloride has the potential to be genotoxic.

In animal experiments employing oral exposure, concentrations of carbon tetrachloride which produced liver tumours were also accompanied by a high incidence of non-malignant liver damage (USEPA, 1995; ACGIH, 1991; CARB, 1986). The USEPA notes that a common biological mechanism: cell death and regeneration, leading to development of the same hepatomas was suggested by observations in the laboratory animal studies they used for the calculation of unit risk. These studies suggest that liver damage may be a precondition for tumour formation resulting from exposure to carbon tetrachloride.

Massachusetts and New York have developed air quality guidelines for long-term exposure based on carcinogenicity as an end-point. Their annual limits of 0.07 $\mu g/m^3$ are based on the inhalation unit risk developed by the USEPA and a individual lifetime risk of $1*10^{-6}$. As discussed above, California developed their unit risk estiamate $4.2*10^{-5}$ from a single mouse study and used this to derive lifetime exposure limits of 0.24 $\mu g/m^3$ and 0.024 $\mu g/m^3$ at lifetime risk estimates of one in one hundred thousand and on in a million respectively.

3.1.2 Regulatory Approaches for Carbon Tetrachloride Based on Non-carcinogenic Endpoints

The ACGIH (1991) developed their occupational standard to prevent liver damage in workers. Both the Commonwealth of Massachusetts and New York State have developed short-term limits was based on the occupational standard. Both agencies employed various safety factors to account for continuous vs non-continuous exposure and exposure to the general population.

It is generally agreed that toxicity to the liver is the most sensitive endpoint for exposure to carbon tetrachloride (USEPA, 1995; ACGIH, 1991; CARB, 1986; Gosselin *et al.*, 1984). Based on the results of separate studies in which rats were exposed orally and via inhalation, it has been suggested that the toxicity of carbon tetrachloride does not depend on the route of exposure (CARB, 1986). As a result, the California Air Resources Board developed their chronic Reference Exposure Level (REL) of 2.4 $\mu g/m^3$ for inhalation from the oral reference dose developed by the USEPA of 0.7 µg/kg/day. It should be noted that although the chronic REL is based on non-carcinogenicity as an end-point, the level at which it is set is comparable to one based on carcinogenicity at a one in one hundred thousand lifetime risk level (2.4 $\mu g/m^3$ over 24-hours is comparable to an annual average of 0.5 $\mu g/m^3$ using a conversion factor of 5, see below)

3.2 Recommendations for Ambient Air Quality Standards for Carbon Tetrachloride

Recommendations for new or revised Ontario Ambient Air Quality Criteria (AAQC) and point of impingement (POI) standards are based upon a weight-of-evidence evaluation of available information. For carbon tetrachloride, liver toxicity is generally agreed to be the most common toxicological effect although toxicity to the central nervous system and kidneys has also been observed. While the USEPA has classified carbon tetrachloride as a probable human carcinogen based on observations of liver tumours in mice and rats exposed to high levels via ingestion, it has been argued that liver damage resulting from carbon tetrachloride exposure is a precondition for tumour development in experimentally exposed animals. As such, basing air quality guidelines on the prevention of chronic liver damage due to long-term exposure should also be protective of the development of cancer.

Of the criteria reviewed from other agencies which are based on a non-carcinogenic endpoint, the (CDHS) was judged to have the most appropriate rationale. The CDHS has proposed a chronic Reference Exposure Level (REL), of 2.4 $\mu g/m^3$ (24-hour average) which is based on the US EPA Reference Dose (RfD) of 0.7 µg/kg/day. While the REL is based on a non-carcinogenic end-

point, the level at which it is set is comparable to one based on carcinogenicity at a one in one hundred thousand lifetime risk level using a unit risk estimate of $1.5*10^{-5}$ developed by the USEPA or $4.2*10^{-5}$ developed by California (Table 1). The Ministry of the Environment therefore recommends that Reference Exposure Limit developed by the developed by the California Department of Health Services be used as the basis for developing a 24-hour average Ambient Air Quality Criterion in Ontario.

The relationship between air quality guidelines of different averaging times is based on empirically derived factors which are used to relate short-term maxima concentrations to long-term averages. The factors are selected to ensure that if the short-term limit is met (e.g. half-hour POI limit or 24-hour AAQC), air quality guidelines based on longer-term exposure will not be exceeded. The factor typically used to convert from an annual average to a 24-hour maxima is 5 while the factor used convert from a 24-hour average to an half-hour maximum is 3 (MOEE 1994c). Depending on the critical end-point being considered other factors may also be employed. In cases where the effects of a contaminant can occur over short-term exposures, like odours, the 24-hour Ambient Air Quality Criterion and the half-hour point of impingement standard may have the same value. Starting with an 24-hour average AAQC of 2.4 µg/m^3 for carbon tetrachloride, the application of a conversion factor of 3 derives a half-hour limit of 7.2 µg/m^3 (Table 2).

Table 2: Recommended AAQC and POI Guideline for Carbon Tetrachloride		
AAQC	24-hour Average	2.4 µg/m^3
POI Guideline	half-hour Average	7.2 µg/m^3

At this time the Ministry is recommending a point of impingement guideline for carbon tetrachloride which will be used to assess applications for certificates of approval involving emissions of carbon tetrachloride. Because of the limited number of sources of carbon tetrachloride in Ontario, and the fact that its use is severely restricted under the federal ozone depleting substances regulations, the development of a point of impingement standard under Regulation 346 is not warranted at this time.

While an the recommended air quality standards for carbon tetrachloride are based on the prevention of adverse health effects in the human population, the potential effects of carbon tetrachloride on other terrestrial biota including plants, soil microbes and herbivores was also examined. With the exception of toxicity studies on experimental animals (mice and rats) very little information is available concerning potential toxicity to other biota. If future studies indicate that the proposed air standards for carbon tetrachloride are not protective of other environmental receptors in Ontario, then the basis on which the standard is established may need to be reviewed.

4.0 Status of Stakeholder Consultations:

In January 1997, the Ministry initiated limited stakeholder consultation on the initial suite of 14 proposed air standards developed under the Standards Plan. The purpose of these consultations was to seek comments from Ontario sources and other stakeholders on the standards proposed During the course of these consultations no specific concerns were identified with respect to the proposed standard for carbon tetrachloride.

Based on an analysis of current Certificates of Approval, the Ministry recognizes that a limited number of sources in Ontario may have predicted ground level concentrations which exceed the proposed point of impingement guideline for carbon tetrachloride. The vast majority of these are for emissions from chemical fume hoods and storage rooms which are typically based on worst-case emission estimates resulting from a spill or handling mishap. Through the implementation of the federal Ozone Depleting Substances Regulations, many of these sources will be required to discontinue using carbon tetrachloride as a laboratory solvent by the year 2000.

5.0 Recommendations:

Based on an assessment of ambient air quality guidelines used in other jurisdiction, the Ministry is proposing to establish:

- a 24-hour Ambient Air Quality Criterion of 2.4 $\mu g/m^3$ to replace the current 24-hour AAQC of 600 $\mu g/m^3$;.

- a point of impingement guideline of 7.2 $\mu g/m^3$ to replace the existing interim point of impingement standard of 1800 $\mu g/m^3$. The point of impingement guideline is based on the proposed 24-hour Ambient Air Quality Criterion and will be used to review and assess applications for Certificates of Approval involving emissions of carbon tetrachloride from new or modified sources.

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7.0 Appendix: Agency-Specific Reviews of Air Quality Guidelines

7.1 Agency-Specific Summary: Federal Government of the United States

1. Name of Chemical: carbon tetrachloride

2. Agency: U.S. Environmental Protection Agency

3. Guideline Value(s):
No ambient air exposure limits are currently promulgated. There is a non-carcinogenic oral reference dose of $7*10^{-4}$ (0.0007) mg/kg/day for chronic oral exposure. As of the current date there is a quantitative estimate of carcinogenic risk from inhalation exposure in the IRIS database (USEPA, 1995). The inhalation unit risk is $1.5*10^{-5}$ (0.000015) tumours per µg/m^3. Using a linearized, multistage extrapolation procedure, this represents an additional risk of 1 in 100,000 per 0.7 µg/m^3 and 1 in 1,000,000 per 0.07 µg/m^3 of lifetime exposure.

4. Application:
IRIS was developed as a source for consistent risk information on chemicals for use in decision-making and regulatory activities. However, values derived and presented in IRIS, in and of themselves, do not represent guidelines or standards. IRIS also contains a summary of current American government regulatory actions under various legislative mandates.

5. Documentation Available:
USEPA, 1995. Integrated Risk Information System (IRIS) Database. U.S. Environmental Protection Agency, Washington, D.C.

Key Reference(s):
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6. Peer Review Process and Public Consultation:
Peer-reviewed scientific research data, analyses and evaluations from various sources, including a variety of public and government agencies from around the world, and the published scientific literature, were employed in the development of these values. Both the general assessment methodologies and the chemical-specific information found in IRIS undergo extensive scientific and policy reviews, within both the USEPA and other science-based U.S. regulatory agencies. Information in IRIS is put forward for use after the results of the public review and comments on draft documents/information have been addressed.

7. Status of Guideline:
There is no current USEPA air quality guideline for carbon tetrachloride in ambient air.

8. Key Risk Assessment Considerations:
The inhalation cancer risk estimates were calculated from oral exposure data in laboratory animals which demonstrated carcinogenicity. The USEPA has classified carbon tetrachloride as B2, a probable human carcinogen. Information from human exposure is considered to be inadequate. According to the USEPA, there have been three case reports of liver tumours developing after carbon tetrachloride exposure. Several studies of workers (Milham, 1976; Blair *et al.*, 1979) who may have used carbon tetrachloride have suggested that these workers may have an excess risk of cancer.

Studies of animal carcinogenicity are considered to be sufficient. Carbon tetrachloride has produced hepatocellular carcinomas in rats (NCI, 1976; 1976a; 1977), mice (Andervont, 1958; Edwards, 1941; Eschenbrenner and Miller, 1943; Edwards and Dalton, 1942; Edwards *et al.*, 1942; NCI, 1976; 1976a; 1977) and hamsters (Della Porta *et al.*, 1961), the species evaluated to date. Sensitivity varied among strains, and trends in incidence appeared inversely related to severity of cirrhosis. All studies were conducted using the oral route of exposure. Data on tumour incidence in four of the studies (Della Porta *et al.*, 1961; Edwards *et al.*, 1942; NCI, 1976; 1976a) were used to calculate oral unit risks, using a linearized, multistage procedure. A geometric mean was calculated from the four unit risks estimates.

Inhalation risk was calculated assuming an air intake of 20 m^3/day and 40% absorption rate by humans (USEPA, 1984). This absorption coefficient was based on 30% inhalation in monkeys and 30% and 57-65% inhalation in humans. A range of estimates of unit risk for inhalation exposures for the four studies cited above was determined, with $1.5*10^{-5}$ per µg/m^3 calculated as the geometric mean for the unit risk.

According to the USEPA, the studies used were all deficient in some respect, precluding the choice of any one study as most appropriate. For all studies, data from males and females were combined because of the small sample sizes. In the first and second studies (Della Porta *et al.*, 1961; Edwards *et al.*, 1942) one dose was tested. Della Porta *et al.* (1961) did not report concurrent control incidence. In the NCI (1976; 1976a) studies, tumour incidence in the mice was virtually 100%, and goodness-of-fit criteria were not satisfied for the multistage model. Tumour incidence in rats in these studies was higher at low doses, presumably because early mortality at higher doses precluded tumour formation. The studies lacked pharmacokinetic data. However, a common biological mechanism, cell death and regeneration, leading to development of the same tumour type, was suggested by observations in all of the studies. Since the risk estimates from these data (across 3-4 species and strains) only vary by 2 orders of magnitude, a geometric mean was derived as the risk estimate to accommodate the several study deficiencies.

The USEPA also calculated an oral reference dose, based on non-carcinogenic effects, using a report published by Bruckner *et al.* (1986). Male Sprague-Dawley rats were given 1, 10 or 33 mg carbon tetrachloride/kg/day by corn oil gavage, 5 days per week for 12 weeks. Liver lesions, as evidenced by mild centrilobular vacuolization and statistically significant increases in serum sorbitol dehydrogenase activity, were observed at the 10- and 33-mg/kg/day doses in a dose-related manner. The lowest-observable effect-level (LOAEL) was therefore established at 10 mg/kg/day (converted to 7.1 mg/kg/day, in order to express the 5-day week experimental results as a daily exposure) and the no-observable-adverse-effect-level (NOAEL) was 1 mg/kg/day (converted to 0.71 mg/kg/day). The NOAEL was divided by 1000 to allow for interspecies and intrahuman variability and extrapolation from subchronic to chronic duration of exposure. The oral reference dose is reported to be $7*10^{-4}$ mg/kg/day. According to the USEPA, subchronic studies in mice gavaged with carbon tetrachloride in corn oil (Condie *et al.*, 1986; Hayes *et al.*, 1985) support the critical effect and the magnitude of the NOAEL and LOAEL found in the rat studies. Additional studies (Alumot *et al.*, 1976; NCI, 1976) in rats lend moderate support to the choice of a NOAEL in the chosen rat study. In addition, the USEPA concluded that the principal study was well conducted and good dose-response was observed in the liver, which is the target organ for carbon tetrachloride toxicity. Four additional subchronic studies support the oral reference dose.

A concentration in the air which would result in the USEPA oral reference dose of 0.0007 mg/kg/day can be calculated using the USEPA exposure default values. Assuming a body weight of 70 kg, the total daily dose is 0.0007 mg/kg/day*70 kg = 0.049 mg/day. Assuming that this is the dose following absorption through the lung and that the lung absorbs 40% of the carbon tetrachloride it is exposed to, the potential dose within the lung is estimated to be 0.049 mg/day÷0.40 = 0.1225 mg/day. Assuming the 70-kg person breathes up to 20 m^3 air/day, and all their exposure to carbon tetrachloride was by air, the air concentration would be 0.1225÷20, which equals 6.125 $\mu g/m^3$ (rounded to 6 $\mu g/m^3$). Using the highest value for absorption in the lung reported by the USEPA (65%), the air concentration would be 3.8 $\mu g/m^3$ (rounded to 4 $\mu g/m^3$). Until a formal inhalation RfC is adopted, the value estimated above should only be considered a provisional value, estimated using available USEPA information and methods.

9. Key Risk Management Considerations:
None, since no guideline for ambient air exists.

10. Multimedia Considerations of Guidelines:
None are reported.

11. Other Relevant Factors:
The publications noted below, as cited in USEPA (1995), indicate other relevant information. Carbon tetrachloride was not mutagenic to either *S. typhimurium* or *E. coli* (McCann *et al.*, 1975; Simmon *et al.*, 1977; Uehleke *et al.*, 1976). At low concentrations, carbon tetrachloride did not produce chromatid or chromosomal aberrations in an epithelial cell line derived from rat liver (Dean and Hodson-Walker, 1979). *In vivo*, unscheduled, DNA synthesis assays have likewise been negative in male Fischer 344 rats (Mirsalis and Butterworth, 1980; Mirsalis *et al.*, 1982). Carbon tetrachloride produced mitotic recombination and gene conversion in *S. cerevisiae*, but only at concentrations which reduced viability to 10% (Callen *et al.*, 1980). Carbon tetrachloride may be metabolized to reactive intermediates capable of binding to cellular nucleophilic macromolecules. Negative responses in bacterial mutagenicity assays may have been due to inadequate metabolic activation in the test systems.

7.2 Agency-Specific Summary: State of California

1. Name of Chemical: carbon tetrachloride

2. Agency: State of California (Office of Environmental Health Hazard)

3. Guideline Value(s):
The non-cancer acute reference exposure level for inhalation is 190 $\mu g/m^3$. A chronic reference exposure level of 2.4 $\mu g/m^3$ is to be used for non-cancer risk assessment. The State of California states that the unit risk of $4.2*10^{-5}$ (0.000042) tumours per $\mu g/m^3$ is to be used for evaluation of cancer risks. This represents an additional risk of 1 in 100,000 per 0.24 $\mu g/m^3$ and 1 in 1,000,000 per 0.024 $\mu g/m^3$ of lifetime exposure.

4. Application:
"The intent of the Committee in developing the guideline was to provide risk assessment procedures for use in the Air Toxics 'Hot Spots' Program." (CAPCOA, 1993). This program is based on a California State law: the Air Toxics 'Hot Spots' Information and Assessment Act of 1987 (Health and Safety Code Section 44360 *et seq*.). The act specifies how local Air Pollution Control Districts determine which facilities in their areas will prepare health risk assessments, how such health risk assessments should be prepared and how the results are to be prioritized. These guidelines were prepared to provide consistent risk assessment methods and report presentation to enable: 1) comparisons between facilities, 2) expeditious review of risk assessments by reviewing agencies, and 3) minimal revisions and resubmittals of risk assessments. The various health-based exposure levels developed for and used in this program should not be employed outside the program's framework. That is to say, the State of California does not consider them to be general, independent, legally enforceable air quality guidelines or limit values at this time.

5. Documentation Available:
CAPCOA, 1993. CAPCOA Air Toxics "Hot Spots" Program. Revised 1992 Risk Assessment Guidelines. Toxics Committee of the California Air Pollution Control Officers Association.

CARB (California Air Resources Board), 1986. Report to the Air Resources Board on Carbon Tetrachloride (Part B): Health Effects of Carbon Tetrachloride. The Epidemiological Studies and Surveillance Section, Department of Health Services. Berkeley, CA.

Key Reference(s):
Edwards, J.E., W.E. Heston and H.A. Dalton, 1942. Induction of the carbon tetrachloride hepatoma in strain L. mice. J. Natl. Cancer Inst., 3:297-30, as cited USEPA, 1995.

Lewis D.C. and G.V. Alexeeff, 1989. Quantitative Risk Assessment of Non-cancer Health Effects for Acute Exposure to Air Pollutants In: Proceedings of the Air and Waste Management Association 82nd Annual Meeting. June 1989, Vol. 89-91. 4 p.

NCI, 1976. Report on the Carcinogenesis Bioassay of Chloroform. National Cancer Institute, Bethesda, MD. March, as cited in USEPA, 1995.

NCI, 1976a. Carcinogenesis Bioassay of Trichloroethylene. National Cancer Institute Carcinogenesis Technical Report Series, No. 2. NCI-CG-TR-2. February, as cited in USEPA, 1995.

NCI, 1977. Bioassay of 1,1,1-Trichlorethane for Possible Carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series, No. 3. NCI-CG-TR-3. January, as cited in USEPA, 1995.

6. Peer Review Process and Public Consultation:
Cancer potency slope factors and acute and chronic reference levels were prepared by the California Office of Environmental Health Hazard Assessment (OEHHA), and these as well as the exposure and health assessments have undergone public review and comment prior to finalization. Peer-reviewed scientific research data were employed in the development of these values. Under the CAPCOA risk assessment process, each assessment is site-specific, and public notice to all exposed individuals is required when the screening process determines that a significant health risk is associated with emissions from a facility. Public input was obtained in identifying and ranking areas and facilities for risk assessment screening and, according to the documentation, additional input is expected as the process moves forward.

7. Status of Guideline:
Current, but updates are possible, with new California risk assessment guidelines being considered in the California Senate.

8. Key Risk Assessment Considerations:
The non-cancer acute reference exposure level for inhalation of 190 $\mu g/m^3$ is based on human respiratory irritation, using the Defined Practical Threshold (DPT) methodology, proposed by Lewis and Alexeeff (1989), which employs the 95% lower confidence estimate on a concentration for a 1% response incidence. This value should protect against perceptible occurrence of observable effects, including irritation, among an exposed human population for a one-hour exposure.

According to CARB (1986), acute, subchronic and chronic studies in humans and laboratory animals indicate that the target tissues for carbon tetrachloride toxicity are the nervous system, the kidney and the liver. Laboratory animal studies have not been conducted that can establish a NOAEL of carbon tetrachloride for biochemical liver changes, the potentially most sensitive endpoint for the evaluation of adverse effects in humans. California indicates that a chronic reference exposure level of 2.4 $\mu g/m^3$ is to be used for non-cancer risk assessment. This was derived by converting the oral acceptable exposure level by assuming a 70 kg person breaths 20 m^3 per day and equal absorption occurs by the oral and inhalation routes. Based on a back

calculation of the California information the estimated oral reference dose was $7.0*10^{-4}$ mg/kg/day.

CARB (1986) concluded that the epidemiological data suggesting an association between carbon tetrachloride exposure and human cancer were inconclusive. Animal studies demonstrated that carbon tetrachloride produces hepatocellular carcinomas in the mouse, rat and hamster. They concurred with the IARC classification, group 2B: probably carcinogenic to humans.

CARB (1986) based its quantitative evaluation of carcinogenicity on two studies of mice (NCI, 1976; 1976a; 1977; and Edwards *et al.*, 1942). For the Edwards *et al.* study, they used a multistage model. For the NCI data, they used a time-to-tumour model. Using the Edwards *et al.* data, they calculated an upper 95% confidence limit unit risk of $4.2 *10^{-5}$. From the NCI data, they calculated an upper 95% confidence unit risk of $9.9*10^{-6}$. According to CARB, the major limitations of the Edwards *et al.* data are the use of only male control mice, the short duration of the experiment and the irregular dosing schedule. Also tumours observed were not classified as benign or malignant. In the NCI study, there was considerable animal mortality and the tumour response was close to 100% in both dose groups, which limited the interpretation of the dose-response curve. The State of California states that the unit risk of $4.2*10^{-5}$ (0.000042) tumours per µg/m^3 is to be used for evaluation of cancer risks. This represents an additional risk of 1 in 100,000 per 0.24 µg/m^3 and 1 in 1,000,000 per 0.024 µg/m^3 of lifetime exposure.

9. Key Risk Management Considerations:
The exposure guidelines were prepared for both non-cancer- and cancer-based endpoints. The cancer-based value is for use in a screening risk assessment to determine the maximum offsite cancer risk for exposed human populations. The process is not readily comparable to the air quality guideline approach to non-carcinogens. The non-cancer guidelines are based on the most sensitive adverse health effect reported in the scientific literature and are designed to protect the most sensitive individuals in the population.

There are options for addressing the possible economic impacts of controlling carbon tetrachloride emissions. It appears that the options are under local control and are based on local risk and socioeconomic analyses, as well as public workshops and hearings. The enforcement mechanism is via operating permits. The process is therefore primarily directed towards site-specific evaluations and development of further regulatory tools, rather than being enforceable levels in and of themselves.

10. Multimedia Considerations of Guidelines:
In the exposure modelling process, non-inhalation pathways should be considered for a number of substances (specified in Table III-5 in CAPCOA, 1993). Carbon tetrachloride is not one of the substances that require non-inhalation modeling. In the California EPA exposure and health assessments it was acknowledged that exposure pathways other than air (e.g., water and food) were possible but that, because of the lack of quantitative information and the predominance of

airborne exposure, other exposure pathways were not considered in the development of the guideline.

11. Other Relevant Factors:

Carbon tetrachloride appears to have genotoxic potential, based on its ability to form reactive intermediates that can covalently bind to DNA; to induce chromosomal rearrangement in fungi *in vitro*; to cause DNA single-strand breaks in rat hepatocyte cells; and to produce morphological transformation of Syrian hamster embryo cells. The absence of positive results in the standard mutagenicity assays indicates that although carbon tetrachloride is potentially genotoxic, it probably does not induce point mutations.

7.3 Agency-Specific Summary: World Health Organization

1. Name of Chemical: carbon tetrachloride

2. Agency: World Health Organization

3. Guideline Value(s):
None

4. Application:
None.

5. Documentation Available:
WHO, 1987. Air Quality Guidelines for Europe. WHO Regional Publications, European Series No. 23. World Health Organization, Regional Office for Europe, Copenhagen, Denmark. 426 p.

Key Reference(s):
None available

6. Peer Review Process and Public Consultation:
None

7. Status of Guideline:
No information

8. Key Risk Assessment Considerations:
No information

9. Key Risk Management Considerations:
No information

10. Multimedia Considerations of Guidelines:
No information

11. Other Relevant Factors:
No information

7.4 Agency-Specific Summary: The Netherlands

1. Name of Chemical: carbon tetrachloride

2. Agency: Netherlands Ministry of Housing, Spatial Planning and the Environment

3. Guideline Value(s):
The target value is 1 $\mu g/m^3$. This is the desired environmental quality goal for air. The maximum emission concentration for airborne effluents from point sources is 7.5 $\mu g/m^3$. The maximum acceptable concentration (MAC, an occupational guideline value) is 12.6 mg/m^3. Carbon tetrachloride is listed as a substance blacklisted for air. Substances blacklisted for air are recommended to be reduced by all available means. A maximum permissible concentration in air of 60 $\mu g/m^3$ has been suggested in van de Plassche, E.J. and G.J.M. Bockting (1993) but the exact status of this guideline is unclear.

4. Application:
Limit values are non-statutory environmental quality objectives that are considered to be policy guidelines. They should not be exceeded and should be considered as requirements to be met. These effects-oriented guidelines may be used simultaneously with source-oriented emission criteria, although it is the latter that are the primary regulatory mechanism for waste flows from point-sources. If effects-oriented guidelines continue to be exceeded, then existing source-oriented emissions criteria will be lowered to bring ambient levels below the effects-oriented guidelines. A maximum acceptable concentration (MAC) is the maximum acceptable concentration of a gas, vapour, or mist of a substance in a workplace.

5. Documentation Available:
Netherlands MHSPE, 1994. Environmental Quality Objectives in The Netherlands. A review of environmental quality objectives and their policy framework in The Netherlands. Risk Assessment and Environmental Quality Division, Ministry of Housing, Spatial Planning and the Environment (MHSPE), The Hague, The Netherlands. 465 p.

NeR Staff Office, 1992. Netherlands Emission Regulations - Air. Netherlands Emission Regulations Staff Office, Bilthoven, The Netherlands. 81 p. + Appendices.

Earlier air criteria documents or more recent integrated criteria documents are available for priority substances such as carbon tetrachloride, but only in Dutch. The following document contains some general information on the processes being considered and provides a maximum permissible concentration for carbon tetrachloride in air, but the regulatory status of this estimate is unclear.

van de Plassche, E.J. and G.J.M. Bockting, 1993. Towards Integrated Environmental Quality Objectives for Several Volatile Compounds. Report No. 679101-011. National Institute of Public Health and Environmental Protection, Bilthoven, The Netherlands. 78 p.

6. Peer Review Process and Public Consultation:
No specific information on this issue was presented in the available English language documentation.

7. Status of Guideline:
Current

8. Key Risk Assessment Considerations:
Carbon tetrachloride is considered to be a carcinogen by the Dutch Government, which recognizes the IARC (1987) classification of carbon tetrachloride as a category 2B carcinogen (inadequate evidence in humans, sufficient evidence in animals). As such it is placed on a priority list of chemicals (SAC) requiring special attention. An integrated criteria document, which contains all relevant data needed to determine any risks, has been prepared, but these documents are only available in Dutch (Netherlands MHSPE, 1994).

9. Key Risk Management Considerations:
National limit values include consideration of environmental, economic and social interests as well as technical options. Specific information on such details was not presented in the available documentation.

10. Multimedia Considerations of Guidelines:
Multimedia exposure was not considered in the development of the current air guideline limits; however, intercompartmental criteria that address this problem are being developed. A maximum permissible concentration in air of 60 $\mu g/m^3$ has been suggested in van de Plassche, E.J. and G.J.M. Bockting (1993) but the exact regulatory status of this suggested guideline is unclear.

11. Other Relevant Factors:
According to the Netherlands (1994), carbon tetrachloride affects the ozone layer and will be reduced as part of their policy on CFCs.

7.5 Agency-Specific Summary: Swedish Institute of Environmental Medicine

1. Name of Chemical: carbon tetrachloride

2. Agency: According to Dr. K. Victorin of the Swedish Institute of Environmental Medicine (pers. comm.), no official Swedish air quality guidelines have been promulgated by the Swedish Environmental Protection Agency.

3. Guideline Value(s):
None

4. Application:
No current guideline

5. Documentation Available:
Victorin, K., 1993. Health effects of urban air pollutants: guideline values and conditions in Sweden. Chemosphere, 27:1691-1706.

6. Peer Review Process and Public Consultation:
No information

7. Status of Guideline:
No current guideline

8. Key Risk Assessment Considerations:
No information

9. Key Risk Management Considerations:
No information

10. Multimedia Considerations of Guidelines:
No information

11. Other Relevant Factors:
No information

7.6 Agency-Specific Summary: New York State

1. Name of Chemical: carbon tetrachloride

2. Agency: New York State

3. Guideline Value(s):
The recommended 1-hour average is 1300 µg/m^3, based on a safety factor of 10 being applied to an occupational exposure guideline. The recommended annual average is 0.07 µg/m^3, based on a unit risk of $1.43*10^{-5}$ (0.0000143) tumours µg/m^3 and a lifetime cancer risk level of $1*10^{-6}$.

4. Application:
". . . they are primarily intended for use in conjunction with the permitting authority and regulatory concerns found in 6NYCRR Parts 200, 201, 212 and 257." (NYDEC, 1991, p. 1). These regulations refer specifically to construction and operation (Certificate to Operate) permits for any sources of air contamination. Rather than being employed as legally enforceable, ambient air quality standards, the guidelines are to be employed to aid in the regulatory decision-making process. This process includes the classification of chemicals into groups of high, moderate and low toxicity. The regulatory screening process considers the toxicity classification and the emission rate potential from a facility. An air emission dispersion model is also specified in the process to guide regulators in their assessment of chemical emissions from sources of interest. Both long-term and short-term effects are considered.

5. Documentation Available:
NYDEC, 1991. New York State Air Guideline -1. Guidelines for the Control of Toxic Ambient Air Contaminants. Draft. New York State Department of Environmental Conservation, Albany, N.Y. 20 p. + Appendices.

6. Peer Review Process and Public Consultation:
The scientific documents prepared by New York State employed peer-reviewed data and models, as well as the professional judgements of its scientific staff. There are opportunities for public comment on guidelines and the guideline development process, but specific information on the process for carbon tetrachloride was not presented in the available documentation.

7. Status of Guideline:
Current

8. Key Risk Assessment Considerations:
No documentation of the risk assessment for the long-term exposure guideline is available. It appears that NYDEC (1991) has classified carbon tetrachloride as a compound of high toxicity, based on its carcinogenicity. Because the long-term guideline of 0.07 µg/m^3 is identical with the USEPA guideline, it can be inferred that New York used the same unit risk $1.5*10^{-5}$. The short-

term guideline was developed by dividing the NIOSH REL-TWA occupational standard by 10. The short-term guideline is intended to protect the public from acute (immediate) adverse effects.

9. Key Risk Management Considerations:
A specific computer model and guidance manual are provided for use of the guidelines in impact screening analyses as employed in the permitting process. The latest version of Appendix B of the New York State Air Guide -1 is dated April 4, 1994.

10. Multimedia Considerations of Guidelines:
Considers human airborne exposure only

11. Other Relevant Factors:
No information is available.

7.7 Agency-Specific Summary: State of Massachusetts

1. Name of Chemical: carbon tetrachloride

2. Agency: Commonwealth of Massachusetts

3. Guideline Value(s):
A 24-hour ceiling limit is 85.52 µg/m^3, based on an extrapolation from an occupational exposure guideline, using a series of uncertainty factors. The allowable ambient limit (AAL) is based on consideration of carcinogenic effects. A unit risk value for carbon tetrachloride of $1.5*10^{-5}$ (0.000015) tumours per µg/m^3 adopted from the USEPA, generates a value of 0.07 µg/m^3 for an annual (1 year) averaging time, using one per million ($1*10^{-6}$) lifetime risk level.

4. Application:
". . . the Division of Air Quality Control, which is responsible for implementing the Department's air programs, plans to employ the AALs in the permitting, compliance and enforcement components of the Commonwealth's air program in general, and the air toxics program in particular." (Commonwealth of Massachusetts, 1990, Volume 1, pg. ix). The primary goal is to "protect the public health and welfare from any air contaminant causing known or potentially injurious effects." The ambient air levels developed in this process should not be considered legally enforceable, air quality standards since they deal only with health-related matters and contain no consideration of technological, economic or enforcement concerns. Rather, they should be employed as guidelines in the development of subsequent regulatory action which does contain a broad consideration of all relevant concerns.

5. Documentation Available:
Commonwealth of Massachusetts, 1990. The Chemical Health Effects Assessment Methodology and the Method to Derive Allowable Ambient Limits, Volumes I and II. Commonwealth of Massachusetts, Department of Environmental Protection, Boston, MA.

Key Reference(s):
ACGIH, 1986. Documentation Of The Threshold Limit Values for Substances in Workroom Air (5th ed.). American Conference of Governmental Industrial Hygienists Inc., Cincinnati, OH.

NCI, 1976. Report on the Carcinogenesis Bioassay of Chloroform. National Cancer Institute, Bethesda, MD. March, as cited in USEPA, 1995.

NCI, 1976a. Carcinogenesis Bioassay of Trichloroethylene. National Cancer Institute Carcinogenesis Technical Report Series, No. 2. NCI-CG-TR-2. February, as cited in USEPA, 1995.

NCI, 1977. Bioassay of 1,1,1-Trichlorethane for Possible Carcinogenicity. National Cancer Institute Carcinogenesis Technical Report Series, No. 3. NCI-CG-TR-3. January, as cited in USEPA, 1995.

Della Porta, G., B. Terracini and P. Shubik, 1961. Induction with carbon tetrachloride of liver cell carcinomas in hamsters. J. Natl. Cancer Inst., 26(4):855-863, as cited in USEPA, 1995.

Edwards, J.E., W.E. Heston and H.A. Dalton, 1942. Induction of the carbon tetrachloride hepatoma in strain L. mice. J. Natl. Cancer Inst., 3:297-301, as cited in USEPA, 1995.

USEPA, 1984. Drinking Water Criteria Document for Carbon Tetrachloride. U.S. Environmental Protection Agency Office of Drinking Water, Washington, D.C. PB86-118155, as cited in USEPA, 1995.

6. Peer Review Process and Public Consultation:
Peer-reviewed scientific research data, analyses and evaluations from various sources, including a variety of public and government agencies from around the world, and the published scientific literature, were employed in the development of these values. Specifically, evidence from the International Agency for Research on Cancer (IARC), the American National Toxicology Program (NTP) and the USEPA was employed. As guidelines, the process used and values generated are not subject to the extensive review and consultation that air quality standards would be subjected to, but external peer reviews were carried out, and public input was solicited through at least two public meetings on the Massachusetts methodology and guideline document (D. Manganaro, Massachusetts Department of Environmental Protection, pers. comm.).

7. Status of Guideline:
Current. Although guideline values are periodically updated, revisions to the current value for carbon tetrachloride are not under consideration (D. Manganaro, Massachusetts Department of Environmental Protection, pers. comm.).

8. Key Risk Assessment Considerations:
The State of Massachusetts has a method of establishing a limit for short-term exposure that assumes the compound has a threshold for adverse effects. In the case of carbon tetrachloride, the 1986 ACGIH occupational limit, reported to be 5 ppm (31.43 mg/m^3), was divided by several factors that attempt to extrapolate from a worker health-based limit to a public limit that protects children and other sensitive individuals. The uncertainty factor incorporates judgments about the amount of information on the toxicity of the compound, the differences between body sizes and weights between adult males and children, and an assumption about the relative contribution of the compound to the total exposure from air. The total uncertainty factor in the case of carbon tetrachloride was 367.5.

Massachusetts cited the USEPA (USEPA, 1984), which derived a unit risk value for carbon tetrachloride of $1.5*10^{-5}$ tumours per $\mu g/m^3$. This unit risk was the geometric mean value from

four animal studies, including two using mice, one using hamsters and one using rats (Della Porta *et al.*, 1961; Edwards *et al.*, 1942; NCI, 1976; 1976a; 1977).

9. Key Risk Management Considerations:
The primary objective of the process is the protection of public health. The Massachusetts system uses hazard assessment only and does not use the number of exposed individuals as a criterion for regulatory action. Furthermore, the selection of the AAL is based on the most sensitive effect. The USEPA's cancer unit risk values and the ACGIH occupational TLV values were adopted for regulation development purposes. For carcinogens, a maximum allowable increase in risk associated with exposure to a chemical was set at one per million ($1*10^{-6}$) for a 70-year lifetime.

10. Multimedia Considerations of Guidelines:
A generic allowance was made for contributions from sources other than respiration: "A relative source contribution factor of 20% is also included to account for sources other than air." (Commonwealth of Massachusetts, 1990, pg. viii).

11. Other Relevant Factors:
None reported